UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,954	12/15/2000	Benjamin F. Cravatt	SCRIP1210-2	1708

7590 06/02/2003

Lisa A. Haile, Ph.D.
Gray Cary Ware & Freidenrich LLP
Suite 1600
4365 Executive Drive
San Diego, CA 92121-2189

EXAMINER	
TRAN, MY CHAU T	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/738,954	CRAVATT ET AL.	
	Examiner	Art Unit	
	My-Chau T. Tran	1639	

-- The MAILING DATE of this communication appears n the cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,32-40 and 42-46* is/are pending in the application.

4a) Of the above claim(s) *1-16,18-31,41 and 47-52* is/are withdrawn from consideration.

5)☒ Claim(s) *43-45* is/are allowed.

6)☒ Claim(s) *17,32-40,42 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *14 April 2003* is: a)☐ approved b)☒ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment filed 3/24/03 in Paper No. 17 is acknowledged and entered. Claims 42 and 44-46 are amended by the amendment.

2. Claims 17, 32-40, and 42-46 are pending.

Drawings

3. The drawings filed on 4/14/03 are acceptable subject to correction of the informalities indicated on the attached "Notice of Draftsperson's Patent Drawing Review," PTO-948. In order to avoid abandonment of this application, correction is required in reply to the Office action. The correction will not be held in abeyance.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code such as pg. 61(paragraph [0148]), pg. 71 (paragraph [0172]), and others throughout the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Withdrawn Rejections

5. The previous rejections 35 USC 112, first paragraph, for claims 44-46 have been withdrawn in view of applicant's argument and amendment to claims 42 and 44-46.

6. The previous rejections under 35 USC 102(b) as being anticipated by Liu et al. (*PNAS*, **1999**, 96(26): 14694-14699) for claims 17, 32-36, 38-40, 42, and 46 have been withdrawn in view of applicant's argument that Liu et al. is not a proper rejection because it is less than one year of the filing date of the application.

7. The previous rejections under 35 USC 102(b) as being anticipated by Zuck et al. (US Patent 4,281,061) for claims 17, 34, and 35 have been withdrawn in view of applicant's argument.

8. The previous rejections under 35 USC 103(a) as being obvious over Liu et al. (*PNAS*, **1999**, 96(26): 14694-14699) in view of Blanchard et al. (US Patent 5,151,164) for claims 17 and 37 have been withdrawn in view of applicant's argument that Liu et al. is not a proper rejection because it is less than one year of the filing date of the application.

9. Upon further consideration, the following new grounds of rejection are made as follows. Therefore, this Office action is a non-final rejection.

10. Claims 17, 32-40, and 42-46 are treated on the merit in this Office Action.

New Rejections

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 17, and 32-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection).

The present claims are directed to determining the presence of active target members of a group of related proteins in each of the plurality of proteomic mixtures in which the related proteins related in having a common functionality for conjugation at an active site and the probe having a reactive functionality specific for the active site. There is no claimed structure or other identifying characteristics presented with respect to the type of "active target members" (e.g. the specific type of protein or the protein sequence) or for that matter the common functionality for conjugation of the probe and the active target members (e.g. the sequence for the binding site of the "active target members" to the probe).

The specification description is directed to the syntheses of a specific probe (e.g. the for biotinylated fluorophosphonate probe such as FP-biotin and FP-peg-biotin) that have specificity toward an "active target member" (e.g. serine hydrolases), which clearly do not provide an adequate representation regarding the open ended claimed the "active target members" (e.g. other type of hydrolases such as glycoside hydrolases or other type of enzymes such as ligases) and the probe specific for other type of "active target members" for the method of the presently claimed invention.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention

involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s) (e.g. all type of protein).

In the present instance, the claimed invention contains no identifying characteristics regarding the "active target members" being detected and the probes specific to the "active target members".

Additionally, the narrow scope of examples directed to specific detection of serine hydrolases and the probe specific to serine hydrolases is clearly not representative of the scope of detecting all type of proteins with any type probe specific to the protein of interest of the presently claimed invention.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 17, 32-40, and 42-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The term "proteomic mixture" of claim 17 is vague and indefinite and confusing with regard to claim 36 "*wherein the proteomic mixture is in an intact cell*". It is unclear as to what is being considered as a "proteomic mixture" (e.g. a mixture of different proteins (see specification pg. 43, paragraph [0112]) or with regard to claim 36 a mixture of cells such as neoplastic sample (see specification pg. 42, paragraph [0111]) wherein each would have different method steps for determining the presence of active target members.

b) The phrase "when active" of claim 17 is vague and indefinite because it is unclear as to the cause of the biological activity of the "target members" in the proteomic mixtures (e.g. absence of an inhibitor or condition of the assay or the binding of the target to the probe).

c) The phrase "said target enzymes" in claim 38 lack antecedent basis.

d) The definition of "X" of claim 38 is vague and indefinite because it is unclear as to how "X" can be a ligand that bind to a complementary (e.g. definition of "reciprocal") receptor in which the receptor is not defined (e.g. is the receptor the target members?), and that "X" can bind to an added ligand (e.g. a ligand binding to a ligand).

e) From definition of the formula (R*(F-L)-X) of the activity-base probe of claim 38, it is unclear as to the binding site for the "active target members" (e.g. "R", "F", or "X").

15. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step(s) is(are): the step(s) of how the probes specific to the "active target members" enter the intact cell in order to conjugate with the "active target members" and how the conjugated probes in the proteomic mixture in the intact cell is determine.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

17. Claim 17 is rejected under 35 U.S.C. 102(e) as being anticipated by Chin et al. (US Patent 6,197,599 B1).

The instant claimed method comprises the following claimed method steps: a) combining each of the proteomic mixtures with at least one probe that is specific to the target members of interest; b) determining the presence of the target members conjugated with the probe in each of the proteomic mixtures.

Chin et al. disclose a method of protein screening (col. 3, lines 4-17). The method (col. 8, claim 2) comprises the following method steps: a) immobilizing a plurality of antibodies on a solid support; b) preparing a mixture (proteomic mixture) containing said first test protein and said plurality of second test proteins; c) applying said mixture to said solid support with immobilized antibodies (probe) and incubating under conditions to permit binding of said second test proteins (target members) thereto (step "a" of the instant claimed method); d) detecting the positions of said first test protein on said solid support thereafter; e) identifying the second test protein from the positions where said first test protein is detected, whereby the interaction between said first test protein and the one or more of said second test proteins is identified (step "b" of the instant claimed method). The antibodies are specific to the protein of interest (col. 5, lines 37-38, and 50-51). Therefore, the method of Chin et al. anticipates the instant claimed method.

18. Claims 17, 32-36, 38-40, 42, and 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al. (*PNAS*, **1999**, 96(26): 14694-14699).

The instant claimed method comprises the following claimed method steps: a) combining each of the proteomic mixtures with at least one probe; b) determining the presence of the target members conjugated with the probe in each of the proteomic mixtures. The activity probe comprise of fluorophosphonate-biotin (FP-biotin).

Liu et al. disclosed a method of activity-based protein profiling using an active site directed probe (Abstract). The probe is a biotinylated fluorophosphonate, FP-biotin, (referring to claims 35, 38-40, 42, and 46) (pg. 14694, left col., lines 30-33). The method steps of reacting protein samples (proteomic mixture) with FP-biotin (activity-based probe) include combining FP-biotin mixture with the protein samples and detecting the FP-biotin-reactive proteins by SDS/PAGE-Western Blotting (pg. 14695, right col., lines 26-64) (referring to claim 17). The FP-biotin-reactive proteins are further analyzed by MALDI mass spectrometry (pg. 14696, left col., lines 11-15) (referring to claims 32-33). FP-biotin can react with numerous serine hydrolyses (target enzyme) in crude cell and tissue samples (pg. 14698, left col., lines 1-8) (referring to claim 36). Therefore, the method of Liu et al. anticipates the claim method.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 17 32-40, 42, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*PNAS*, **1999**, 96(26): 14694-14699) and Blanchard et al. (US Patent 5,151,164).

The instant claimed method comprises the following claimed method steps: a) combining each of the proteomic mixtures with at least one probe; b) determining the presence of the target members conjugated with the probe in each of the proteomic mixtures. The method step further comprise of analyzing for the presence of proteins conjugated with the probe using capillary electrokinetic analysis. The activity probe comprise of fluorophosphonate-biotin (FP-biotin).

Liu et al. disclosed a method of activity-based protein profiling using an active site directed probe (Abstract). The probe is a biotinylated fluorophosphonate, FP-biotin, (referring to claims 35, 38-40, 42, and 46) (pg. 14694, left col., lines 30-33). The method steps of reacting protein samples (proteomic mixture) with FP-biotin (activity-based probe) include combining FP-biotin mixture with the protein samples and detecting the FP-biotin-reactive proteins by SDS/PAGE-Western Blotting (pg. 14695, right col., lines 26-64) (referring to claim 17). The FP-biotin-reactive proteins are further analyzed by MALDI mass spectrometry (pg. 14696, left col., lines 11-15) (referring to claims 32-33). FP-biotin can react with numerous serine

hydrolyses (target enzyme) in crude cell and tissue samples (pg. 14698, left col., lines 1-8) (referring to claim 36).

Liu et al. does not expressly disclose that the protein is detected by capillary electrokinetic analysis.

Blanchard et al. disclose an apparatus for improving the capillary electrophoretic processes (col. 2, lines 21-23). The capillary electrophoresis apparatus can be employed in the electrophoretic resolution of a wide variety of solutions and suspension including protein and polypeptides (col. 3, lines 51-68). The enhanced capillary zone electrophoretic apparatus and process would provide low volume capability, high separation efficiency, and sensitive detection scheme.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include capillary electrokinetic analysis as taught by Blanchard et al. in the method of Liu et al. One of ordinary skill in the art would have been motivated to include capillary electrokinetic analysis in the method of Liu et al. for the advantage of low volume capability, high separation efficiency, and sensitive detection scheme (Blanchard: col. 3, lines 65-68). Since both Liu et al. and Blanchard et al. disclose a method of detecting protein by electrophoresis (Liu: pg. 14695, right col., lines 26-64; Blanchard: col. 3, lines 51-68).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999.

The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct
May 30, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER